October 19, 1953

Dr. Daniel Mazia
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Dear Dr. Mazia:

Thank you for your reprints as just received. I am sorry not he have been better acquainted at an earlier date (namely for a review in Physiol, Rev.) with your experimental essays at a genetic transduction in amphibian eggs. I certainly agree that this line of approach has not been adequately tested, with suitable material on which appropriate selection methods can be exercised, to rule out the possibility that such transductions can occur. They seem to be cropping up all the time in various bacteria, as a separate phenomenon from the more familiar sexual process so far established only in strainskel? Escherichia coli.

I was visiting Berkeley in August, and looked for you, but of course missed you. I would have welcomed an opportunity to talk over this problem of transduction in higher organisms. It is obvious that the optimal system has yet to be worked up.

May I suppose that no sore detailed interpretation of the specific inhibitory effects of DNA on development has been formulated? I note your suggestion (p.29 of the paper in Growth Symp.) that such inhibitory effects might apply to bacterial transductive systems but have been overlooked. I do not think they could have been overlooked, unless you would demand the presistent presence of large excess of the active material. As you point out, the reversibility of the inhibition by DNA is already distinctive as compared with the irreversible transductions of bacteria. I rather suspect, however, that the genetic alterations are not fixed in the treated cell, but only in later clonal progeny. In Salmonella, we have a sytem involving the transduction of motility to non-motile mutants: this is symmimes abortive so that a motile cell, swimming out into a selective, soft agar, leaves behind a long trail of non-motile descendants. The pattern suggests that each division of the motile bacterium engenders one motile, one non-motile daughter; i.e., the transduced genetic material functions but does not proliferate. The more usual pattern is, however, a stable alteration regularly transmitted in hereddit.

Please pardon my insittence on the transduction terminology. I can't help feeling that the fuzzy connotations of "directed mutation" and "transformation" helped to impede the proper abalysis of the pneumococcus story from a genetic view-point for at least two decades after its discovery by Griffith in 1928. [But one might argue that had the geneticists gotten an early hold, they would never have allowed the chemists to discover the role of DNA.]

Yours sincerely,

Joshua Lederberg Associate Professor of Genetics